CLINICAL DIAGNOSIS AND THE LABORATORY:

LOGICAL STRATEGIES FOR COMMON MEDICAL PROBLEMS

PAUL F. GRINER
ROBERT J. PANZER
PHILIP GREENLAND

CLINICAL DIAGNOSIS AND THE LABORATORY

Logical Strategies for Common Medical Problems

PAUL F. GRINER, M.D.

Samuel E. Durand Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

ROBERT J. PANZER, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

PHILIP GREENLAND, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

This work was supported, in part, by grants from the Rochester Area Hospitals' Corporation and The Henry J. Kaiser Family Foundation.



YEAR BOOK MEDICAL PUBLISHERS, INC.
Chicago • London • Boca Raton

Copyright © 1986 by Year Book Medical Publishers, Inc. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior witten permission from the publisher. Printed in the United States of America.

2 3 4 5 6 7 8 9 0 CY 89 88 87

Library of Congress Cataloging-in-Publication Data Main entry under title:

Clinical diagnosis and the laboratory.

"This work was supported, in part, by grants from the Rochester Area Hospitals' Corporation and the Henry J. Kaiser Family Foundation."

Includes bibliographies and index.

1. Diagnosis, Laboratory. I. Griner, Paul F. II. Panzer, Robert J. III. Greenland, Philip. IV. Rochester Area Hospitals' Corporation. V. Henry J. Kaiser Family Foundation. [DNLM: 1. Diagnosis, Differential. 2. Diagnosis, Laboratory. QY 4 C641] RB37.C57 1986 616.07'5 85-20249 ISBN 0-8151-4004-5

Sponsoring Editor: Richard H. Lampert Manager, Copyediting Services: Frances M. Perveiler Production Project Manager: Max Perez Proofroom Supervisor: Shirley E. Taylor

Contributors

Dean A. Arvan, M.D.

Professor of Pathology University of Rochester School of Medicine and Dentistry Rochester, New York

Edgar R. Black, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

James L. Budd, M.D.

Instructor in Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Julia Connelly, M.D.

Assistant Professor of Medicine University of Virginia School of Medicine Charlottesville, Virginia

Susan C. Day, M.D.

Assistant Professor of Medicine Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

James G. Dolan, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

John M. Eisenberg, M.D.

Sol Katz Associate Professor of General Medicine Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

Margaret A. Fallon, M.D.

Assistant Professor of Pathology and Laboratory Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Philip Greenland, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Paul F. Griner, M.D.

Samuel E. Durand Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

William J. Hall, M.D.

Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Jeffrey T. Holt, M.D.

Staff Fellow National Institute for Heart, Lung and Blood Diseases National Institutes of Health Bethesda, Maryland

Seth M. Kantor, MD

Associate Professor of Medicine The Ohio State University Columbus, Ohio

Anthony L. Komaroff, M.D.

Associate Professor of Medicine Harvard Medical School Brigham and Women's Hospital Boston, Massachusetts

Anthony F. Lehman, M.D.

Assistant Professor of Psychiatry University of Rochester School of Medicine and Dentistry Rochester, New York

Raymond J. Mayewski, M.D.

Associate Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Richard F. McNamara, M.D.

Instructor and Fellow in Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Alvin I. Mushlin, M.D.

Associate Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Rudolph J. Napodano, M.D.

Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Fitzhugh C. Pannill III, M.D.

Assistant Professor of Medicine University of Wisconsin Medical School Milwaukee, Wisconsin

Robert J. Panzer, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Daniel H. Ryan, M.D.

Assistant Professor of Pathology University of Rochester School of Medicine and Dentistry Rochester, New York

Martin F. Shapiro, M.D.

Assistant Professor of Medicine UCLA School of Medicine Los Angeles, California

Mark H. Stoler, M.D.

Instructor and Fellow in Pathology University of Rochester School of Medicine and Dentistry Rochester, New York

Anthony L. Suchman, M.D.

Assistant Professor of Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Thomas G. Tape, M.D.

Instructor and Fellow in Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

David C. Wilbur, M.D.

Assistant Professor of Pathology and Laboratory Medicine University of Rochester School of Medicine and Dentistry Rochester, New York

Foreword

There is a science to the art of medicine. There is method in the hunch, the flash of intuition, and the "index of suspicion."

Much of this clinical method has to do with the particularization, to a specific patient, of our prior experiences with large numbers of other but similar patients. No wonder, then, that the strategies and tactics for dealing with large numbers—the strategies and tactics of epidemiology and biostatistics—have helped us understand and improve clinical method.

Nowhere is this understanding better seen than in diagnosis: the effort to recognize the class or group to which a patient's illness belongs so that based on our prior experience with that class, the subsequent clinical acts we can afford to carry out, and the patient is willing to follow, will maximize that patient's health. Whether by diagram, sensitivity and specificity, likelihood ratio, Bayes's theorem, test and test-treatment threshold, or multivariate analysis, we have come to prescribe (if not yet perfectly describe) the diagnostic process in a fashion that multiplies rather than dismisses the hunch of the seasoned clinician, and expands rather than compresses the diagnostic information contained in quantitative laboratory data.

The authors of this book have been leaders in this exciting movement. Their supplement to the October

x Foreword

1981 issue of *Annals of Internal Medicine* not only demonstrated the utility of a quantitative approach to diagnosis; its clarity and relevance made it the most frequently requested supplement ever produced by that journal.

Now they are back again, this time with a version that is expanded (to cover additional disorders) and extended (to identify the preferred diagnostic routes). Both we and our patients are the better for it.

DAVID L. SACKETT, M.D.
Professor of Clinical Epidemiology
and Biostatistics
Professor of Medicine
McMaster University
Hamilton, Ontario

Preface

This book is the product of an effort that grew out of a meeting held in the spring of 1980 by an ad hoc committee of the American College of Physicians. The committee, chaired by Dr. Ceylon Lewis, was exploring initiatives that the College might undertake to stimulate cost containment in health care. On the premise that cost containment should be a natural by-product of sound clinical reasoning, the committee decided to sponsor an article that would reinforce the important principles governing the use of diagnostic tests and procedures. A contract was made with the faculty of the General Medicine Unit of the Department of Medicine at the University of Rochester School of Medicine and Dentistry to develop the article. With the help of grants to the College from the National Fund for Medical Education, The Henry J. Kaiser Family Foundation, and The Commonwealth Fund, we prepared a manuscript on the "Selection and Interpretation of Diagnostic Tests and Procedures: Principles and Applications" that was published as a supplement to the Annals of Internal Medicine in October 1981 (94:553-600, 1981). That this supplement met an apparent need was suggested by a request for more than 10,000 reprints within the first year of its publication.

The impetus for further work came from the comments of many interested readers who indicated that

the application of the important principles of test selection and interpretation was limited by a lack of readily available information about discriminating characteristics of many of the tests and procedures commonly used in the practice of internal medicine. Clearly, the rate of growth of diagnostic technology was exceeding the ability of physicians to keep up with some of these developments, particularly in the fields of imaging and specialized biochemical tests. We thus decided to develop a manual that would provide information on the role of the diagnostic tests and procedures available for many of the commonly considered clinical problems in adult medicine, information necessary for logical and efficient diagnostic strategies. We were assisted in this effort by a major grant from the Rochester Area Hospitals' Corporation. The grant helped us identify important content areas through a survey of practicing physicians to determine which clinical problems posed the greatest difficulty for them, difficulty arising from a lack of knowledge of the available diagnostic tests and their utilities. The grant provided funds to develop and pilot the early phases of our book on the floors and in the clinics of the hospitals in Rochester. Feedback resulting from this early work by medical students, residents, and attending physicians led to significant changes aimed at making the book more useful. We are grateful to Dr. James Block, president, and Dr. Donna Regenstreif, senior vice president, of the Rochester Area Hospitals' Corporation for their encouragement and support of this phase of the book's development.

This book has been designed to provide information leading to preferred diagnostic strategies for some of the most commonly considered clinical problems in adult medicine, problems that often require the use of tests and procedures. While using this book, the reader (medical students and residents, in particular) should bear in mind some important considerations. First, since most diagnoses can be made without the use of laboratory tests or procedures, the value of a compre-

hensive history and physical examination cannot be overemphasized.

Second, a few words should be said about the way in which the information contained in this book is expressed and the limitations of this information. Such terms as predictive value, prior probability, and posterior probability (terms commonly used in the current literature) are replaced by pretest and posttest probabilities or odds throughout. It must be recognized that the calculations leading to these probabilities are based on values for test characteristics (i.e., sensitivity and specificity) and pretest probabilities that are often estimates at best. The literature is replete with data concerning test characteristics that are suspect because of methodologic biases. Additionally, physicians vary widely in their accuracy in predicting the likelihood of a disease on the basis of clinical (i.e., nonlaboratory) information. Another point to be made is that many of the calculations in the book assume the results of various tests to be independent, an assumption that may not be valid for many combinations of tests. Also, most of the material presented in this book does not deal with the diagnostic value of the degree of abnormality of a biochemical test or the reliability of the interpretation of a procedure, factors that obviously influence the probabilities for or against a particular diagnosis.

Third, diagnostic technology is changing rapidly. Very possibly, one or more chapters in this book may become dated by new technology. The development of a new test may lead to major changes in test selection and alter an overall diagnostic approach.

Fourth, when physicians process sequential information leading to impressions for or against a specific diagnosis, they may not follow the reasoning inherent in the Bayesian approach to decisions used in this book.

Fifth, this book deals with only a small proportion of the clinical problems that physicians encounter or consider in the course of their hospital rounds or office practice.

All of these observations lead us to the central point of this book, which is that a systematic approach to the integration of clinical information with the knowledge available about diagnostic tests and procedures is more important than a precise, accurate estimate of a posttest probability of disease. If this book results in the reader becoming more organized in his or her approach to diagnosis, addressing the purpose of a test before it is ordered, asking how the result will influence diagnosis or management, and showing the logic of a sequential (as opposed to a scatter-shot) approach to the ordering of tests and procedures, it will have served its primary purpose.

Another purpose of this book is to show that a readily available and organized clinical data base can facilitate accurate diagnosis. In this respect, the book can be viewed as an intermediate step toward a more efficient data base. Already, one of the editors (R. J. P.) and a few residents and attendings at two of the hospitals in Rochester have programmed microcomputers to process the data contained in this book to both facilitate its retrieval and provide a more dynamic, interactive approach to patient management and medical education. Ultimately, we envision information of this kind being available to the practicing physician through a desk top computer to facilitate the process of clinical diagnosis and patient management.

The editors are indebted to the following physicians for the valuable comments and suggestions they provided from their review of individual chapters: John Amatruda, Robert Betts, John Clough, Jules Cohen, Peter Dans, Wallace Epstein, Stephen Goldfinger, William Hall, Robert Hamill, Robert Heinig, William Hood, Richard Hornick, Robert Hull, Anthony Komaroff, Marshall Lichtman, Victor Marder, Albert Mulley, David Ransohoff, Robert Schapiro, Donald Schoch, and Harold Sox. The editors would also like to thank

David L. Sackett, M.D., Professor of Clinical Epidemiology and Biostatistics and Professor of Medicine at McMaster University in Hamilton, Ontario, for writing the foreword.

Grateful appreciation is also extended to Marilyn Owens, Joan Hutton-Steward, and Nancy George for the quality and tirelessness of their work in preparing the material for this book and readying it for the publisher.

PAUL F. GRINER, M.D.

Contents_____

1 / Principles of Test Selection and Use	1
Raymond J. Mayewski, Alvin I. Mushlin, Paul F. Griner	
2 / Principles of Test Interpretation	17
Paul F. Griner, Raymond J. Mayewski	
3 / Odds and Likelihood Ratios	36
Anthony L. Suchman, James G. Dolan	
4 / Sore Throat in Adult Patients	44
Anthony L. Komaroff	
5 / Infectious Mononucleosis	57
Paul F. Griner	
6 / Coronary Artery Disease	68
Philip Greenland	
7 / Myocardial Infarction	36
Philip Greenland	
8 / Syncope)7
Susan C. Day, John M. Eisenberg	
9 / Infective Endocarditis	23
Philip Greenland	
10 / Hypertrophic Cardiomyopathy	1 0
Philip Greenland	
11 / Deep Venous Thrombosis	52
Rudolph J. Napodano	
12 / Pulmonary Embolism	58
Raymond J. Mayewski	
13 / Pleural Effusions	33
William J. Hall	

xviii Contents

14 / Chiomic Obstructive I unitoliary Disease.			•	•		201
Raymond J. Mayewski						
15 / Mediastinal Mass						215
Thomas G. Tape, Paul F. Griner						
16 / Sarcoidosis	·		,	÷	٠	229
Raymond J. Mayewski						
17 / Cholelithiasis	×					247
Paul F. Griner						
18 / Obstructive Jaundice						256
David C. Wilbur, Dean A. Arvan						
19 / Acute Viral Hepatitis	•	•	ž			270
Jeffrey T. Holt, Dean A. Arvan						
20 / Hepatic Metastases		:•1				284
Robert J. Panzer						
21 / Acute Pancreatitis	٠	*	•	٠		297
Mark A. Stoler, Dean A. Arvan						
22 / Complications of Acute Pancreatitis			•			308
Robert J. Panzer						
23 / Pancreatic Cancer				٠		318
Robert J. Panzer						
24 / Acute Diarrhea	٠	×				333
Anthony L. Suchman, Paul F. Griner						
25 / Acute Dysuria in Adult Women						346
Anthony L. Komaroff						
26 / Microscopic Hematuria	٠	×	•	٠		366
Julia Connelly, Paul F. Griner						
27 / Urinary Incontinence	•		:•;			377
Fitzhugh C. Pannill III, Alvin I. Mushlin						
28 / Impotence			•	٠	٠	398
Edgar R. Black						
29 / Normal Pressure Hydrocephalus	٠	÷				413
Richard F. McNamara, Robert J. Panzer						
30 / Depression	٠		•			423
Anthony F. Lehman, Martin F. Shapiro						
31 / Iron Deficiency Anemia		٠	•	ě	•	431
Paul F. Griner						
32 / Erythrocytosis		•		×	. 4	442
James L. Budd, Philip Greenland						

	Conte	ents	xix
33 / Coagulation Disorders			. 459
Anthony L. Suchman, Paul F. Griner			
34 / Erythrocyte Sedimentation Rate			. 476
Daniel H. Ryan, Dean A. Arvan			
35 / Temporal Arteritis			. 491
Seth M. Kantor			
36 / Systemic Lupus Erythematosus			. 504
Paul F. Griner			
37 / Breast Cancer			. 518
Alvin I. Mushlin			
38 / Hypercalcemia			. 531
Margaret A. Fallon, Dean A. Arvan			
39 / Hypercortisolism (Cushing's Syndrome)		. 546
Edgar R. Black, Alvin I. Mushlin			
40 / Hyperthyroidism and Hypothyroidism			. 558
James G. Dolan			
41 / Thyroid Nodules	* * *		. 573
James G. Dolan			
42 / Glossary			. 588
Index			. 590

Chapter	1
---------	---

Principles of Test Selection and Use*

Raymond J. Mayewski, M.D. Alvin I. Mushlin, M.D. Paul F. Griner, M.D.

PURPOSES OF TESTS AND PROCEDURES

Diagnosis of Disease

The process of diagnosis requires two essential steps. The initial step is the establishment of diagnostic hypotheses followed by attempts to reduce their number by progressively ruling out specific diseases. This process requires very sensitive tests. Such tests, when results are normal, permit the physician confidently to exclude the disease. The next step is the pursuit of a strong clinical suspicion. This process requires a very specific test. Such a test, when results are abnormal, should essentially confirm the presence of disease.

The intelligent selection of an appropriate laboratory test thus depends upon the proper test for the

*Reproduced with permission of the *Annals of Internal Medicine* (Griner P.F., et al.: Selection and interpretation of diagnostic tests and procedures: Principles and applications. 94:553–600, 1981).